b.) Remarks

Claims 23 and 71-80 remain rejected under 35 U.S.C. §103(a) as being obvious over Greenlee (U.S. Patent Publication No. 2003/0139395) in view of Suzuki (U.S. Patent No. 5,543,415) and Goodman & Gilman (The Pharmacological Basis for Therapeutics (2001) 469). According to the Examiner, Greenlee teaches use of adenosine A_{2A} receptor antagonists in treating anxiety disorders, Suzuki teaches an antidepressant composition containing (E)-8-(3,4-dimethoxystyryl)-1,3-diethyl-7-methylxanthine, and Goodman & Gilmans shows antidepressants can treat generalized anxiety disorders.

In response to the same rejection, Applicants previously showed that Istradefylline is unexpectedly superior over adenosine A_{2A} receptor antagonists that are structurally similar to those taught in the Examiner's prior art.

For instance, from the results of test example 1, Istradefylline at 3 mg/kg po shows vastly more potent activity on the change of the number of head-dips than Compound C[1] at 10 mg/kg po. (Compare Table 1-A at page 50 with Table 1-C at page 51). Similarly, test examples 4 and 6 show the effects of Istradefylline on the Elevated Plus-Maze and Social Interaction tests are vastly more potent than those of Compound C. (Compare Table 3-A at page 55 with Table 3-C at page 56, and compare Table 4-A at page 56 with compare Table 4-C at page 57).

As discussed previously, Compound C is a compound having Greenlee's triazolopyrimidine skeleton. Therefore, the record conclusively establishes the superiority of Istradefylline over the prior art for treating generalized anxiety disorder (claims 23 and

[1] 5-amino-2-(2-furyl)-7-[4-(3-hydroxy-3-methylbutyl)piperazinyl][1,2,4]traizolo[1,5-c]pyrimidine, see page 40.

71), obsessive-compulsive disorder (claim 73), panic disorder (claim 75), agoraphobia (claim 77), and social phobia (claim 79).

In response to Applicants' showings, the Examiner provides bases of rejection at pages 3-4 of the Office Action. These are essentially the same as was discussed previously. As to Applicants' previous argument, the Examiner's answer is provided at page 2 wherein the Examiner states Applicants' comparison is to "vehicle" and not to Greenlee specifically.

First, as to Greenlee, Applicants wish to explain that Compound C is a compound structurally similar to those taught by Greenlee.

Second, as to "vehicle", Applicants next wish to further explain it is entirely conventional in the pharmaceutical art, when comparing the results of test runs (for evaluating the effects of drugs), to standardize each result to the vehicle value. That is, efficacy is normally presented as percent improvement over vehicle, just as was done here.

This is seen, for one example, in Shiozaki et al., Actions of adenosine A_{2A} receptor antagonist KW-6002 on drug-induced catalepsy and hypokinesia caused by reserpine or MPTP, *Psychopharmacology*, Vol. 147 (1999) 90-5, copy attached. Therein, the effects on locomotor counts are evaluated by standardization with the vehicle-treated (normal) group. See p. 93 right column, lines 3-20 and Fig. 3. For the Examiner's information, it is desired to standardize data with the vehicle value to compare the effects of drugs among different test runs, especially if the vehicle value is different among the test runs. Moreover, it should be understood that if compounds were not compared to

vehicle, then direct comparisons would needlessly have to be made anew every time a new compound was evaluated.

Nonetheless, for the Examiner's convenience, a suitable Declaration by Dr. Tomoyuki Kanda is attached to complete the record.

In view of the above remarks and accompanying Declaration, Applicants submit that all of the Examiner's concerns are now overcome and the claims are now in allowable condition. Accordingly, reconsideration and allowance of this application is earnestly solicited

Claims 23, 25 and 71-80 remain presented for continued prosecution.

Applicants' undersigned attorney may be reached in our New York office by telephone at (212) 218-2100. All correspondence should continue to be directed to our below listed address.

Respectfully submitted,

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